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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/859,651 | 05/17/2001 | Vitaliy A. Kordyum | PHAGE.001DV1 | 3897 |

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KNOBBE MARTENS OLSON & BEAR LLP
2040 MAIN STREET
FOURTEENTH FLOOR
IRVINE, CA 92614

| EXAMINER | |
|---|---|
| LEFFERS JR, GERALD G | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1636 | |

DATE MAILED: 12/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/859,651 | KORDYUM, ET AL. | |
| | Examiner | Art Unit | |
| | Gerald G Leffers Jr., PhD | 1636 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *10 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *41-47,49-53,55-58 and 60-64* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *49-52,58 and 60-62* is/are allowed.

6)☒ Claim(s) *41-47,53,55-57,63 and 64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. §§ 119 and 120**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

Receipt is acknowledged of an After-Final amendment, filed 11/10/03, in which claims were amended (claims 53, 55, 58 and 60) and claims were cancelled (claims 54 and 59). The proposed amendment has been entered into the file. Upon further review of the pending cases before the office and issued files, it is apparent that obviousness double patenting issues exist that must be addressed before issuance of some of the pending claims from the instant application. Therefore, prosecution of the instant application is hereby reopened.

Any rejection of record not addressed herein is withdrawn. Claims 41-47, 49-53, 55-58, 60-64 are pending and under consideration in the instant application.

### *Double Patenting*

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ormum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 41-47, 53 and 55-57 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 of U. S. Patent No. 6,642,026. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons. **This is a new rejection.**

Claims 1-10 of the '026 patent are directed to a method for producing a biologically active human acid fibroblast growth factor protein, comprising transforming an *E. coli* host cell with a plasmid comprising an expressible gene encoding the growth factor protein and subsequently infecting the transformed cell with a strain of bacteriophage λ, wherein the bacteriophage is capable of mediating delayed lysis of the host cell, and growing the infected cells under culture conditions that induce lytic growth without lysis until a desired level of production of the growth factor protein as soluble and biologically active protein is reached. The phage λ can comprise a temperature sensitive $cI^{857}$ mutation (claim 2) and the infected cells grown for a period of time between 20-37°C (claim 3). The phage λ can have additional mutations in genes that mediate delayed lysis (claim 4), selected from the group of N, Q and R genes (claim 5). The host cell can be deficient for a suppressor of amber mutations (claim 7) or produce the suppressor (claim 6). Multiplicity of infection can range from about 1 to about 100 phage per targeted host cell (claim 8), or from about 10 to about 25 phage per host cell (claim 9). The phage-mediated lysis of the host cells can be delayed at higher multiplicities of infection relative to lower multiplicities of infection (claim 10). The portions of the specification that provide support for the cited claims teach embodiments featuring the use of phage λ $cI^{857}$ $Q^{am117}$ $R^{am54}$ to infect cells transformed with a plasmid expressing a eukaryotic gene encoding aFGF. The phage particles used were generated from a lysogenic host strain by cultivating the lysogen at permissive temperatures (i.e. shift to 43°C) (e.g. Example 2). Interferon α-2b is a eukaryotic protein exemplified as produced using the claimed methods (e.g. Figure 10).

The rejected claims are drawn to a method for producing a biologically active protein comprising transforming an *E. coli* host cell with a plasmid having at least one copy of an

expressible eukaryotic gene encoding the protein, lytically infecting the transformed bacterial host cell with a bacteriophage λ phage having a temperature sensitive mutation and at least one mutated gene selected from the group consisting of N, Q & R genes, culturing the E. coli host cell at temperatures of less than about 32°C that delay lysis of the host cells permitting the production of the biologically active protein (e.g. claim 53). The temperature-sensitive mutation can be $cI^{857}$ (claim 55). The host cell can express a suppressor for the mutations (e.g. claim 41), or alternatively, the host cell can lack a suppressor for repairing amber-mutations (claim 56). The host cell can be recombinase deficient (i.e. recA-). Certain embodiments are drawn to the use of a phage λ $cI^{857}$ $Q^{am117}$ $R^{am54}$ strain (e.g. claim 41).

Claims 1-5 and 7 of the '026 patent anticipate claims 53, 55-56 of the instant application and thus necessarily make obvious those claims. With regard to the recA deficient host cell, such cells are commonly used for the maintainence and expression of vector DNAs in E. coli and would be *prima facie* obvious for practicing the methods of instant claims 53, 55-56. With regard to embodiments directed to phage λ $cI^{857}$ $Q^{am117}$ $R^{am54}$, it would have been obvious to use any strain exemplified in the '026 patent as featuring delayed lysis of host cells under appropriate conditions. With regard to the use of lambda lysogenic strains to produce phage particles for use in the claimed methods, it would have *prima facie* obvious to do so because the working examples supporting the claims recited in the '026 patent use this approach.

Claims 41-47, 53, 55-57 and 63-64 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11, 19 and 24 of copending Application No. 09/929,918. Although the conflicting claims are not identical,

they are not patentably distinct from each other because of the following reasons. **This is a new rejection.**

Claims 1-11, 19 and 24 of the '918 application are directed to a method for producing a biologically active protein comprising transforming a strain of *E. coli* with a plasmid having at least one copy of an expressible gene encoding a biologically active protein, operably linked to a T7 polymerase promoter, wherein the transformed bacterial host cell is capable of expressing the T7 RNA polymerase, infecting the transformed host cell with a bacteriophage λ capable of mediating delayed lysis of the host cell and cultivating the host cell under a culture condition that induces growth of the cell without lysis and producing the protein as a soluble, biologically-active protein (claim 1). The bacteriophage can have a temperature-sensitive mutation (claim 2), which mutation can be a $cI^{857}$ mutation (claim 3). The infected host cells can be grown at temperature that prevents lysis of the host cell (claim 4). The phage λ can have additional mutations in genes that mediate delayed lysis (claim 5), which genes can be selected from the group of N, Q and R genes (claim 6). The host cell can either produce (claim 7) or be deficient for a suppressor of amber mutations (claim 8). The multiplicity of infection can be from about 1 to about 100 (claim 9), or from about 10 to about 25 (claim 10). The delayed lysis can be delayed at higher multiplicities of infection relative to lower multiplicities of infection (claim 11). The phage particles used in the method can be generated by inducing the lytic growth of an E. coli host cell comprising a λ lysogen (e.g. claim 24). The portions of the specification that provide support for the cited claims teach embodiments featuring the use of phage λ $cI^{857}$ $Q^{am117}$ $R^{am54}$ to infect cells transformed with a plasmid expressing a eukaryotic gene encoding aFGF. The phage particles used were generated from a lysogenic host strain by cultivating the lysogen

at permissive temperatures (i.e. shift to 43°C) (e.g. Example 2). Interferon α-2b is a eukaryotic protein exemplified as produced using the claimed methods (e.g. Figure 10). Claim 19 is directed to the production of human interferon.

Claims 1-11, 19 and 24 of the '918 application anticipate the rejected claims of the instant application and thus necessarily make obvious those claims. With regard to the recA deficient host cell, such cells are commonly used for the maintainence and expression of vector DNAs in *E. coli* and would be *prima facie* obvious for practicing the methods of the instant claims. With regard to embodiments directed to phage λ $cI^{857}$ $Q^{am117}$ $R^{am54}$, it would have been obvious to use any strain exemplified in the '026 patent as featuring delayed lysis of host cells under appropriate conditions.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 42 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 42 is vague and indefinite in that it is unclear what human "alpha-2b" protein is intended. It appears for reading the specification and from claim 52 that the word "interferon" should follow the word "alpha-2b" in claim 42.

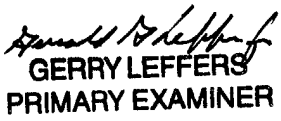
***Conclusion***

Claims 41-47, 49-53, 55-58 and 60-64 are pending in the instant application. Claims 41-47, 53, 55-57 and 63-64 are rejected. Claims 49-52, 58 and 60-62 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald G Leffers Jr., PhD whose telephone number is (703) 308-6232. The examiner can normally be reached on 9:30am-6:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (703) 305-1998. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.




Gerald G Leffers Jr., PhD
Primary Examiner
Art Unit 1636

Ggl